Constituents of Umbelliferous Plants

XVI.* Terpenoids from the Root of Selinum carvifolium L.

JOHN LEMMICH, PETER ALSTED PEDERSEN, MANOHAR SINGH SOOD** and BENT EICHESTEDT NIELSEN

The Royal Danish School of Pharmacy, Chemical Laboratory B, DK-2100, Copenhagen, Denmark

The ether extract of the root of Selinum carvifolium L., in addition to the terpene, 1,1,5-trimethyl-2-formyl-4-(3-acetoxyethyl-2-butenyloxy)-cyclohexadiene-(2,5) (I), previously isolated from this plant,1 afforded the terpenes (III), (IV), and (V).

(III) is shown to be 1,1,5-trimethyl-2-formyl-6-((E)-3-acetoxyethyl-2-butenyloxy)-cyclohexadiene-(2,4). (IV) and (V) are shown to be the parent alcohols of (I) and (III), respectively. As in the case of (III), the acid moiety of (I) is shown to possess the configuration E.

In view of our continued interest in constituents of umbelliferous plants and prompted by the recent isolation of the ester terpenes (I) and (II) from the root of Selinum carvifolium L. by Bohlmann and Grenz,1 we report on the isolation of some related terpenes from Selinum carvifolium L. and present additional data. In particular, a new ester terpene (III) and two terpene alcohols (IV) and (V) have been isolated in addition to (I), whereas we found no evidence, in our root material of Selinum carvifolium L., of the ester terpene (II).

In addition, the compounds (VI) – (VIII), as well as 2,3,4-trimethyl-benzaldehyde and 2,3,4-trimethylbenzoic acid were isolated, all being artifacts, formed during the isolation procedure by degradation of the genuine terpenes. Thus, (VI) and (VII) were formed by air oxidation of the alcohols (IV) and (V), respectively. Formation of the methyl ethers (IX) and (X) was observed, if the plant extract was dissolved in 90 % methanol and defatted with petroleum ether.

The ester terpene (I), an optically active liquid, on treatment with sulfuric acid in methanol solution afforded 2,3,4-trimethylbenzaldehyde and the methyl ether (X), as also described by Bohlmann and Grenz.1 In addition, the reaction mixture afforded an acid (VIII), the constitution and configuration of which


was evident from its degradation by alkaline hydrolysis to the known hydroxy acid (XI) and its formation by mild acetylation of (XI). The conclusion that (I) was 1,1,5-trimethyl-2-formyl-4-((E)-3-acetoxyethyl-2-butenoyloxy)-cyclohexadiene-(2,5) was substantiated by the $^1$H NMR- and mass spectra, which, in turn, were in accord with the data given by Bohlmann and Grenz for (I), and, furthermore, by the UV- and IR-spectra.

The ester terpene (III) is an optically active liquid. The UV- and IR-spectra of (III) indicated that it was an $\alpha\beta, \gamma\delta$-unsaturated aldehyde. Treatment of a methanol solution of (III) with sulfuric acid yielded 2,3,4-trimethylbenzaldehyde, the acid (VIII), and the methyl ether (X). These results are in accord with the structure 1,1,5-trimethyl-2-formyl-6-((E)-3-acetoxyethyl-2-butenoyloxy)-cyclohexadiene-(2,4) for the terpene (III). The $^1$H NMR- and mass spectra supported this assignment. The $^1$H NMR-data showed the expected similarities to those recently reported by Bohlmann and Grenz for 1,1,5-trimethyl-2-formyl-6-(2-acetoxyethyl-2-butenoyloxy)-cyclohexadiene-(2,4), isolated from Silaum sila S. et T.

The terpene alcohols (IV) and (V) are optically active liquids, which by UV-, IR-, $^1$H NMR-, and mass spectrometry were shown to be the parent alcohols of (I) and (III), respectively. On oxidation, (IV) and (V) afforded the known ketoaldehyde (VI) and the ketoaldehyde (VII). A mixture of terpenes including (IV) and (V) was recently obtained from Silaum sila S. et T., and their separation, after conversion to the acetates, was reported. The genuine mixture of alcohols afforded $^1$H NMR-data, which are in accordance with those stated in this paper for the separate compounds (IV) and (V).

**EXPERIMENTAL**

Melting points, UV-, IR-, and $^1$H NMR-spectra (CCl$_4$) were determined as described in previous papers. The mass spectra were recorded on a Varian Mat CH-5 instrument (direct inlet) at 70 eV; ion source temperature 100°; sample temperature 10–60°; ionization.
current 100 μA; m/e values and intensities of peaks higher than 15 % (for compound (III) 5 %) of base peak, and of a few less intense, but pertinent peaks, are stated. Microanalyses were performed by Dr. A. Bernhardt, Eibach über Engelskirchen. The silica gel (Merck 0.05–0.20 mm) used in column chromatography was activated at 120° overnight and impregnated with 10 % of water. The optical rotation values were determined on a Perkin-Elmer Polarimeter, Model 141.

The plant material was collected in September near Copenhagen. The dried and ground roots (840 g) on extraction with ether, and subsequent evaporation of the solvent, afforded 30 g of extract, which was chromatographed on 400 g of silica gel. The sequence of eluents was petroleum ether, to which increasing amounts of ether were added (10–50 %), petroleum ether–ether (1:1) containing 20 to 100 % of ethyl acetate, and finally, ethyl acetate, to which increasing amounts of methanol were added. Fractions containing the compounds (IV) and (V) were rechromatographed on silica gel, using benzene, to which ethyl acetate (10–20 %) was added, as eluent.

The following compounds (a–h) were obtained (described in order of elution): a. 2,3,4-Trimethylbenzaldehyde. A colourless liquid, b.p. 122–123°/11 mm (Ref. 6, b.p. 121°/11 mm). The 1H NMR-spectrum and the analytical data were consistent with the assigned structure. The following derivatives were prepared: the 2,4-dinitrophenyl-hydrazone, m.p. 234–235° (methanol) (Ref. 3, m.p. 223°; Ref. 7, m.p. 227–229°); the oxime, m.p. 130–131° (aq. ethanol) (Ref. 6, m.p. 131–132°); and by air oxidation, 2,3,4-trimethylbenzoic acid, m.p. 169–169.5° (aq. ethanol) Ref. 8, m.p. 167.5°. The analytical data of the derivatives were in accord with the values calculated.

b. 1,1,5-Trimethyl-2-formyl-cyclohexadiene-(2,5)-one-4 (VI). A yellow crystalline compound, m.p. 58–59° (petroleum ether). The UV, IR, 1H NMR-, and mass spectra were in accordance with the data given by Bohlmann and Zdero.4

c. 1,1,5-Trimethyl-2-formyl-cyclohexadiene-(2,4)-one-6 (VII). A yellow liquid, which crystallizes upon standing, m.p. 25–30°. UV: λmax (EtOH) 316 nm (3.98) shoulders at λ 302 nm (3.90) and 332 nm (3.82). IR: 2710, 1685 (CHO), 1665 (CO), 1575 (conj. C=C).

1H NMR-data (δ values): doublets at 6.84 (1H) (Jbc = 6 cps), 1.96 (3H) (Jcd = 1.5 cps), and a multiplet at 7.03 (1H) are assigned to the protons b, d, and c, respectively, a singlet at 9.44 (1H), to the aldehyde proton α, and a singlet at 1.37 (6H), to the gem-dimethyl protons f. Mass spectrum (sample temp. 10–15°): 164 (M+, 100), 149 (19), 136 (99), 135 (96), 121 (52), 108 (15), 107 (30), 95 (15), 93 (89), 91 (71), 79 (23), 77 (43), 67 (18), 65 (26), 53 (21), 51 (22), 41 (35), 39 (40).

d. 1,1,5-Trimethyl-2-formyl-(E)-3-acetoxyethyl-2-butenyloxy-cyclohexadiene-(2,5) (I). A viscous liquid (1.3 g), [α]D = +257° (c 1.2, CCl4). (III) is unstable even when stored at −20°. Partly deteriorated samples, upon rechromatography afforded samples of (III) with lower rotation values, presumably as a consequence of optical instability. UV: λmax (EtOH) 226 nm (4.43), IR: 2710, 1710 (CHO), 1740, 1215 (CH3COO−), and 1650 cm−1 (C=C). The 1H NMR- and mass spectra were in accordance with the data given by Bohlmann and Grenz.1

e. 1,1,5-Trimethyl-2-formyl-(E)-3-acetoxyethyl-2-butenyloxy-cyclohexadiene-(2,4) (III). A viscous liquid (1.3 g), [α]D = +257° (c 1.2, CCl4). (III) is unstable even when stored at −20°. Partly deteriorated samples, upon rechromatography afforded samples of (III) with lower rotation values, presumably as a consequence of optical instability. UV: λmax (EtOH) 226 nm (3.94), IR: 3380 (OH), 2720, and 1690 cm−1 (CHO). The 1H NMR-spectrum was in accordance with the data given by Bohlmann and Grenz.1 Mass spectrum (sample temp. 10–15°): 166 (M+, 47), 151 (17), 137 (100), 123 (80), 122 (20), 121 (20), 109 (15), 108 (36), 107 (20), 105 (26), 95 (18), 91 (22), 79 (22), 77 (37), 69 (15), 67 (17), 55 (16), 53 (19), 51 (17), 43 (37), 41 (31), 39 (37).

Oxidation of (IV) (1 mg in 0.2 ml CCl4) with MnO2 (1 h, at room temperature) yielded the ketoaldehyde (VI), identified by TLC and UV-spectroscopy.

g. 1,1,5-Trimethyl-2-formyl-cyclohexadiene-(2,4)-ol-6 (V). An oily liquid (0.2 g), [α]D20 +45° (c 1.0, CHCl3). UV: λmax (EtOH) 305 nm (3.97). IR: 3420 (OH), 2710, 1870 (CHO), and 1570 cm⁻¹ (conj. C=C). The 1H NMR-spectrum was in accordance with the data given by Bohmann and Grenz. Mass spectrum (sample temp. 10 – 15°): 166 (M⁺, 17), 161 (5), 148 (7), 137 (47), 133 (27), 124 (15), 123 (100), 122 (21), 121 (20), 120 (17), 119 (17), 109 (20), 107 (17), 105 (33), 95 (24), 91 (26), 84 (74), 83 (20), 79 (20), 77 (29), 70 (22), 69 (15), 67 (21), 55 (34), 53 (18), 45 (16), 43 (94), 42 (15), 41 (40), 39 (35). Air oxidation of (V) yielded the ketoaldehyde (VII), identified by TLC and UV-spectroscopy.

h. (E)-3-Acetoxyethyl-2-butenanoic acid (VIII). Colourless needles, m.p. 56 – 57° (petroleum ether-ether). (Found: C 53.37; H 6.38. Calc. for C9H14O3: C 53.16; H 6.37.) UV: λmax (EtOH) 215 nm (4.12). IR: 1725, 1222 (CH₂COO⁻), 1636 (C = O), and 1645 cm⁻¹ C=C. The NMR-data (CDCl₃, δ values): a broad singlet at 11.73 (1H), which disappears upon exchange with D₂O, is assigned to the proton m. A broad pattern at 5.92 (1H) is assigned to the proton n, a slightly broadened singlet (2H) at 4.65 to the protons p, and a slightly broadened singlet (6H) at 2.15 to the methyl protons o and r.

Saponification of (VIII). A solution of (VIII) (80 mg) in 0.2 N ethanolic potassium hydroxide (8 ml) was kept at 40° for ½ h. The reaction mixture was worked up using a column extraction technique previously described. (E)-3-Hydroxyethyl-2-butenanoic acid (XI) (56 mg), m.p. 110.5 – 111° (petroleum ether-ethyl acetate) was obtained. The analytical data were in accordance with the composition C₉H₁₄O₃. UV: λmax (EtOH) 216 nm (4.09) (Ref. 2, m.p. 113°). The NMR-spectrum of (XII) shows four singlets, at 219 nm (4.13).

Acetylation of (XI). A solution of (XI) (20 mg) in a mixture of acetic anhydride (0.2 ml) and pyridine (0.3 ml) was kept at room temperature for ½ h, and then one drop of water was added. Upon evaporation of the solvents, the residue was chromatographed on silica gel (5 g). The eluent was benzene-formic acid (100:0.2) in which increasing amounts of ethyl acetate (20 – 50%) were added. 27 mg of (XII) were obtained as a colourless oil. Crystallization from petroleum ether-ether yielded needles with m.p. 55 – 56°. The IR-spectrum was identical with that of the sample of (VIII), described above.

Treatment of (III) with sulfuric acid. A solution of (III) (150 mg) in a mixture of methanol (3 ml) and 4 N sulfuric acid (0.2 ml) was kept at 50° for 10 min. The reaction mixture was diluted with water (3 ml) and extracted with a mixture of benzene and chloroform. The benzene-phases was washed with washed with 12 mg hydrogen carbonate solution, dried, and evaporated to dryness. The residue (68 mg) was chromatographed on silica gel (5 g) using petroleum ether-ether mixtures as eluents. 2,3,4,5-Tetramethylbenzaldehyde (19 mg) and an optically inactive methyl ether (X) (14 mg) with 2H NMR-spectrum (EtOH) 306 nm (4.03) were obtained. The 1H NMR-spectrum of (X) was in accordance with the data given by Bohmann and Grenz. The water phase and the sodium hydrogen carbonate phase, mentioned above, were mixed and worked up, using the column extraction technique, described above. (E)-3-Acetoxyethyl-2-butenanoic acid (VIII) (53 mg), which after recrystallization melted at 54.5 – 56° (petroleum ether), was obtained.

Treatment of (I) with sulfuric acid. A solution of (I) (63 mg) in a mixture of methanol (2 ml) and 4 N sulfuric acid (0.2 ml) was kept at 50° for 2 min. Using the procedure described above the following compounds were obtained: 2,3,4-trimethylbenzaldehyde, the methyl ether (X), and the acid (VIII) (m.p. 53 – 54°, petroleum ether-ether).

1,1,5-Trimethyl-2-formyl-4-methoxy-cyclohexadiene-(2,5) (IX). When the extract was dissolved in 90% methanol and defatted with petroleum ether, the defatted extract, in addition to the above mentioned compounds a–h, yielded (IX). (IX) is an optically inactive, viscous liquid. UV: λmax (EtOH) 224 nm (3.92). The NMR-spectrum (δ values: a doublet at 9.41 (1H) is assigned to the aldehyde proton a (JHCH = 0.7 cps), a doublet at 6.49 (1H) (JCH = 4 cps) to the proton b, a multiplet at 4.48 (1H) to the proton c, a perturbed doublet at 1.74 (JCH = ca. 1 cps) to the methyl protons d, a slightly broadened singlet at 5.40 (1H) to the proton e, and singlets at 3.06, 1.24, and 1.19 (3H each) to the methoxy protons s and the gem-dimethyl protons f, respectively. The long range coupling between the aldehyde proton a and the proton e was confirmed by decoupling experiments.

Acknowledgements. The authors are grateful to Dr. Elfinn Larsen, Chemistry Department, Danish Atomic Energy Commission Research Establishment, Risø, Denmark, for the measurements of the mass spectra. Thanks are due to the Danish Natural Science Research Council for placing an NMR-spectrometer at the disposal of this Laboratory.
REFERENCES

8. Jacobsen, O. Ber. 19 (1886) 1209.

Received July 9, 1970.